Sialadenitis and Major Salivary Gland Tumors in Children

Experience at Los Angeles Childrens Hospital and a Review of the Literature

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■ *Except for mumps, the benign lesions most frequently seen in the salivary glands of a child are parotitis, hemangioendotheliomas and mixed tumors. Carcinoma and sarcoma are uncommon. Rapid growth and pain are features of malignant change.*

Chronic parotitis usually subsides under conservative treatment. If operation is necessary, total parotidectomy is advisable. Scout x-ray films and sialangiographic examination are useful in differentiating an inflammatory lesion from a neoplastic growth.

The treatment of choice for a non-inflammatory tumor is surgical excision, for most parotid tumors are radioresistant. Small masses should be completely excised for pathological evaluation. Since operation entails risk of damage to the seventh nerve, incisional biopsy may occasionally be indicated in the case of a large diffuse lesion for it is very likely to be benign and operation unnecessary. The risks of seventh nerve damage are magnified in a child as the anatomic structures are smaller and the nerve lies in a more superficial position.

ON REVIEW OF THE records of 95 patients with major salivary gland problems admitted to the Los Angeles Childrens Hospital from 1948 to 1963 (Table 1), it was noted that except for obvious inflammation or infectious parotitis, the major reason for seeking medical attention was the presence of a non-tender, parotid lump or swelling.

Differentiating a neoplastic growth from chronic asymptomatic parotitis can be a difficult problem. For the most part, in the pediatric age group the lesions in the major salivary glands are of an acute or chronic inflammatory variety. They may be initially painless and grow slowly. Parotid tumors are seen in newborn babies and infants but are more common in older children. Salivary gland tumors can be found in aberrant locations—in the lips, the cheek, the palate and the floor of the mouth.

In children the leading cause of death under 14 years of age is accidents, but malignant disease leads in the five to nine year age bracket.[13] Rush and coworkers[16] noted that, excluding tumors of the brain and eye, more than 8 per cent of tumors in children are in the head and neck area, the most common sites being the skin, nasopharynx, thyroid and salivary glands. Lymphomas, neuroblastomas and reticuloendotheliosis are common secondary lesions in this region.

Reiquam[15] presented 20 cases of salivary gland tumors in children, 13 of which the lesions were hemangiomas. Howard[10] reported on 21 cases of parotid tumors in children and included five hemangioendotheliomas. He presented six cases of mixed tumor and on reviewing the literature from

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TABLE 1.—*Major Salivary Gland Disease in Children—Etiologic Findings in 95 Cases at Childrens Hospital, Los Angeles*

Mumps (excluded)	36
Chronic Parotitis	18
Acute Parotitis	24
Submaxillary Gland Sialadenitis	9
Tumors	4
Hemangiomas	4

1920 to 1949 noted that of 2,309 patients with mixed tumor only 66 were children. In 50 of the 66 cases the tumor was benign and in 11 cases malignant. Reiquam's review of 132 cases of papillary cystadenoma lymphomatosum showed only four cases in children. Twenty of the 132 lesions were benign, including 11 hemangioendotheliomas and six mixed tumors. Five of 14 carcinomas in the parotid were mucoepidermoid. Four undifferentiated carcinomas were noted and in children they appeared to be much more aggressive tumors than in the adults. Death from metastasis is most common from this tumor.

Byers and Ackerman[3] reported 24 cases of salivary gland tumors in children and 17 were mixed tumors. Bhaskar[1] reviewed 2,500 salivary gland tumors at the Armed Forces Institute of Pathology and found 27 cases in children. There were 22 juvenile hemangiomas, three lymphangiomas and two xanthomas. The Cancer Memorial Hospital experience in New York City[4] was limited in that only two of 233 pediatric head and neck tumors evaluated were tumors of the salivary gland.

Present Series

Parotitis.—There were 78 cases of parotitis seen at Childrens Hospital from 1948 to 1963. Thirty-six cases were diagnosed as mumps and the patients were discharged to the infectious disease ward at the Los Angeles County Hospital or to their homes. There were 18 cases of chronic parotitis, including three cases of tuberculosis, one of parotid cyst and one due to cat scratch fever. The cases of tuberculosis occurred in children two to three years of age. In only five of the cases of chronic parotitis was biopsy done and none of the patients had subtotal parotidectomy. The clinical course and the sialogram indicated conservative therapy with antibiotics and observation as the rule. The age span of onset was from seven months to 18 years. There was no predominant side of involvement, and in four cases both sides were involved. The most common symptom was an asymptomatic firm swelling which in several cases was recurrent. In all but one case the lesion subsided with time.

There were 24 cases of acute parotitis, of which two were postoperative. Two-thirds were in males, and the right side was involved twice as often as the left. Staphylococcus aureus was isolated in 10 cases, streptococcus in one and pneumococcus type III in another. One of the two patients with postoperative parotitis had had orchidopexy; and the other, who died four days after operation, had had pyloromyotomy for pyloric stenosis. Two of the 24 patients had a recent history of mumps. Nine infants had acute parotitis at one month of age or less, and two were affected at birth. The remainder were older. In nine cases incision and drainage was necessary because of fluctuation and pointing; and in four of the nine the patient was one month or less in age. No further therapy was required in any of this group. The common factor in the children less than one month of age appeared to be dehydration secondary to diarrhea, vomiting or other factors leading to dehydration or cachexia.

Hemangioma.—There were four cases of parotid hemangioma in the series, and in girls. In all cases the lesion was first detected at birth or within the first six months. One patient had had a parotid swelling since birth, with an overlying area of telangiectasia. A right subtotal parotidectomy was done at eight weeks of age with incomplete excision of the lesion. A persistent seventh nerve palsy was noted after operation. X-ray therapy was used at eight months of age and a 3 × 4 cm mass was still present when the patient was last observed at five years of age. In another case a parotid swelling developed when the child was five months of age, after an upper respiratory infection. The lesion was excised at 14 months of age without complication, recurrence or seventh nerve injury. The third child was treated conservatively for parotid hemangioma on the right side that had begun when the patient was less than one year of age. Ligation of the external carotid artery, radiation therapy and subsequent injection of sclerosing solutions were carried out. A 3 × 4 cm mass was still present at eight years of age and a resection was planned. The fourth case was in an eight-month-old white girl who had had red discoloration at the angle of the right jaw since birth. A mass that first appeared at six months of age grew to 4 × 6 cm within two months. Subtotal paroti-

dectomy was done on October 11, 1963, with preservation of the facial nerve. The patient recovered without facial paralysis.

Submaxillary Gland.—Nine cases of submaxillary problems were reviewed. All of the lesions were of an inflammatory nature and no neoplastic growths were detected. Two sublingual gland cysts were marsupialized into the oral cavity. One 11-year-old child had a calculus removed from the Wharton's duct on the left. Three children had incision and drainage for a submaxillary abscess and two had excision of the gland for what appeared on sectioning to be an infectious granulomatous inflammation.

Parotid Neoplasms.—Four cases were reviewed. Abstracts of the records follow:

CASE 1. A six-year-old boy was admitted in January, 1961. A mass had been present in the right parotid gland for one month. Soon after admission the patient had total parotidectomy with sacrifice of the seventh nerve. The pathologist reported a malignant mixed tumor with neurofibrosarcoma as a major element. Microscopically there were elongated cells with fibrillar processes extending in various directions. There was a definite tendency to palisading. The nuclei were spindle shaped and vesicular. The patient was treated postoperatively in March, 1961, with 1,650 roentgens. He died at home in November, 1961, with extensive involvement of the face and oral cavity in neoplastic growth.

CASE 2. An eight-year-old white boy was admitted in October, 1951, with a three-week history of a $4 \times 4 \times 3$ cm mass in the area of the right parotid gland. The tumor was resected, including the seventh nerve, and postoperative radiation was given. The pathologist reported a malignant mesenchymal tumor, probably in the nature of a neuroblastoma or neurosarcoma. The child subsequently received radiation therapy but died of extensive local disease on April 17, 1952.

CASE 3. A girl 18 months of age when first seen in July, 1946, had an irregular soft mass 1 cm in diameter that had been present since birth in the right parotid area. It was soft, movable and felt as if it contained many cysts. When she was five years of age, the tumor involved the right cheek and right ear. Several areas of skin pigmentation overlay the tumor. There were *cafe-au-lait* spots over the body. In 1949 a large portion of the mass was excised and the patient had facial palsy thereafter. The pathologist reported the lesion was a plexiform neurofibroma. In July, 1957, radical excision of the tumor of the cheek and neck was carried out, and at that time the tissue showed considerable variation in nuclear size with hyperchromatism. There was increased cellularity with frequent mitotic figures. In comparison with previous specimens, there was a definite transition to a sarcomatous pattern. Over the succeeding 10 years, excisions with plastic procedures were carried out at yearly intervals. When last seen at 17 years of age the patient was married, had a child and was free of disease.

CASE 4. The patient, a 15-year-old white girl, first noted a non-tender movable mass at the angle of the right mandible in July, 1957. It had not increased in size and was asymptomatic. On examination a 2×3 cm firm movable mass was felt below the right ear lobule without significant enlargement of adjacent lymph nodes. In February, 1958, subtotal parotidectomy on the right side was carried out. The facial nerve was not injured. The pathologist reported the mass to be a well encapsulated $2.5 \times 2 \times 1.5$ cm nodule made up in part of large areas of loose myxomatous tissue. There were small nests of epithelial cells scattered throughout. The diagnosis was benign mixed tumor of the parotid gland. When the patient was last seen in December, 1963, there was no evidence of recurrence.

Differentiation of Inflammatory Lesions from Neoplasms

A common problem in managing parotid swellings in children is the differentiation of an inflammatory lesion from a neoplasm. Since operation entails considerable risk of injury to the seventh nerve, every effort should be made to make sure it is necessary.

An inflammatory process is obvious when tenderness, pain, swelling, erythema, fever, drainage of purulent material from Stensen's duct and systemic reactions such as debility or malaise are present. Acute parotitis is seen most frequently after infections about the head and neck after general infectious diseases with septicemia and pyemia, after dehydration and cachexia following operative procedures, and in the course of chronic parotitis. The most common offending organisms are staphylococci, streptococci and pneumococci. The treatment is conservative and consists of local hygienic measures, application

of compresses and administration of specific antibiotics. Incision and drainage is a necessity if the course of the disease fluctuates widely, and it may be indicated if infection appears to be progressive.

In taking a history, care should be taken to determine whether the parotid swelling is the first such instance or is a recurrent flare-up of inflammation. The swelling in chronic parotitis usually subsides completely at the end of an attack, but there may be some persistent enlargement and a history of recurrences. The disease can recur at intervals of weeks to months, and the attacks last from days to weeks. It occurs more frequently in children than in adults but may be found at any age. Fever, when it occurs with chronic parotitis, is usually of a mild degree and there is usually little constitutional disturbance. Roentgenographic studies rarely show parotid calculi. Sialographic examination may help to establish a diagnosis.[19]

For sialangiography, after the child is sedated a small lacrimal canula is inserted into the Stenson duct orifice and about 0.5 ml of a warm solution of contrast medium (Lipiodol®) is injected slowly. In most cases the ductal system is normal, but sialangiectasis may be present as indicated by a beaded appearance similar to that noted in bronchiectasis (Figure 1). This is most often a primary or congenital lesion and is fairly diagnostic of chronic parotitis. A diseased gland will usually take more contrast material than a normal gland. A further value of this examination is that the films may show any intraglandular or extraparotid growth that is causing pressure on the ductal system.

Etiology and Treatment of Chronic Parotitis

The cause of chronic parotitis in children is not known but infection secondary to a ductal obstruction is thought to be a common etiologic factor. Poor oral or general conditions, mucosal atrophy and glandular abnormalities are all involved. The gland may be involved as part of a secondary process from a generalized disease, as in sarcoid, lymphoma or tuberculosis. In children allergic disease and sensitivity to drugs have been incriminated.[14] Some of the drugs which may cause parotitis are mercury, lead, copper, iodine, nicotine and opium. Among food substances, spinach, pork, lemons, grapes, oranges, acidic foods, iodized salt and tuna fish have been inculpated.[2]

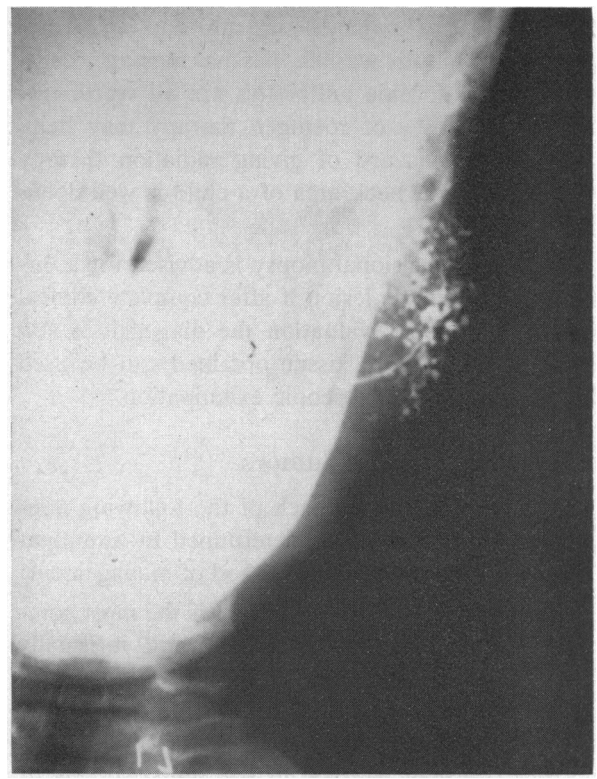

Figure 1.—Sialogram showing classic sialangiectasis in a seven-year-old boy who had chronic parotitis on the left side.

Dorrance[5] put emphasis on conservative management of chronic parotitis. In the majority of cases the disease subsides without operation. However, if severe disability and frequent attacks indicate operation, total parotidectomy is advisable.[6,15] Perineural adhesions are commonly encountered and the task of dissection is a painstaking one. If the deep lobe is left behind, salivary fistulas may occur or parotitis recur. Seventh nerve dissection is extremely hazardous should a secondary procedure become necessary.

One point to be emphasized with regard to parotidectomy in infants is that the mastoid process is not completely pneumatized and the stylomastoid foramen is in an unprotected and exposed position on the lateral skull surface. The nerve is only 0.5 mm in diameter, lies nearer the surface than in adults and can be easily injured.

Radiation therapy has been advised. However, it is difficult to destroy infectious activity in the parotid radiation. Furthermore, if it is used the mucous membranes of the soft palate, the mouth and pharynx will atrophy and the drying may be more uncomfortable than the parotid problem.[8]

In conservative management, oral and dental hygiene with mouth washes, passive massage, compresses and specific antibiotics are all worth trying. Small doses of roentgen therapy may help, although the hazard of giving radiation therapy in the head and neck area of a child is well documented.

Needle or incisional biopsy is advised for a diffuse asymptomatic lesion if after complete clinical and radiographic evaluation the diagnosis is still not established. The tissue obtained can be used for culture and microscopic examination.

Non-Inflammatory Tumors

The specific type of each of the following non-inflammatory tumors, as determined by examination of tissue, decrees the method of management:

Hemangiomas.—Hemangioma is the most common vascular tumor in children and it usually appears in the first year of life. Parotid hemangioma is more frequent in girls than in boys and in Caucasians than in persons of other races. It may show a transient increase in size during crying or straining, and when palpated may feel soft to firm. A bluish discoloration to the skin may be evident, this symptom depending on the amount of cavernous component present. Most tumors of this order are capillary hemangiomas without a true capsule. They tend to be lobulated.

Microscopically one sees solid sheets and masses of cells and anastomosing capillaries replacing parotid acinar structures leaving widely separated ducts. Silver stains for reticulum demonstrate the epithelial nature of the cells in the solid areas,[12] distinguishing it from a hemangiopericytoma, as the latter occurs entirely outside the reticulum sheet of the vessels.[17] The two common features are the formation of atypical epithelial cells in greater numbers than are required to line the vessels with a simple epithelial membrane, and the formation of vascular tubes with a delicate framework of reticulum fibers. The linings of the tubes have a decided tendency to anastomosis. Sialograms may show a distorted duct pattern. Malignant change is extremely rare.

Many kinds of therapy have been reported, including surgical excision, massage, radiation, implantation of radon seeds, use of sclerosing agents, carbon dioxide snow and ligature of external carotid artery. In some cases no treatment is given but the patient is kept under observation. There is no report of a complete spontaneous regression of a parotid hemangioma. If delay is possible, surgical treatment should not be carried out until the patient is at least six months of age. Rapid growth and recurrence have been observed in infants operated upon when younger. There is a tendency as the patient gets older for the tumor to have a capillary pattern and less cellularity and mitoses, this change being associated with a slower growth potential.[18]

As to the hazards of parotidectomy, Wolfe[20] in a review of the literature recorded 4 per cent mortality (two of 46 patients) and facial nerve injury in 25 per cent of cases.

Lymphangiomas.[1,9]—Lymphangiomas are uncommon in the parotid gland except by extension from the cervical area. Rare cases have been presented in which the tumor was confined to the parotid gland due to sequestered intraparotid lymphatic anlagen. Lymphangiomas are multiloculated and composed of cystic spaces of varying size. Microscopically the cysts are composed of randomly arranged intracommunicating and dilated lymphatic channels with a flattened epithelial lining of the walls. The lesions are usually slow-growing, but rapid enlargement may follow an upper respiratory tract infection. Surgical operation is considered the treatment of choice. Radiation and radon seeds are of doubtful value

Benign Mixed Tumors

Mixed tumors are common in adults, infrequent in children. Of a total of 2,309 cases of mixed tumor reviewed by Howard,[10] only 66 (less than 3 per cent) were in children. Many of these tumors are contained in a thin delicate capsule consisting of connective tissue and remnants of compressed salivary gland tissue. In reviewing the history of cases in which there was recurrence, it was noted that in almost 80 per cent of them the tumor had been broken into at time of operation. These tumors can be round, smooth and movable or nodular and fixed and the most frequent location is the tail of the parotid gland beneath the lobule of the ear. The size varies from 4 mm to 10 cm. Histologic examination often reveals excrescences 1 mm or less in diameter which jut through the capsule. This explains the presence of multiple local recurrences. When seen primarily the mass is usually solitary; lesions of recurrence are usually multiple. It has been noted that the re-

currence rate after removal of mixed tumor is in the neighborhood of 20 or 30 per cent.

The growth rate of these tumors is variable. They may remain static as a painless lump for long periods or they may rapidly increase in size. Local pressure may cause discomfort or pain. Not often if the lesion is benign is there involvement of the seventh nerve. Ninety per cent of them are in the parotid gland, about 10 per cent are in the submaxillary gland and less than 1 per cent in the sublingual gland. The median age of patients is 42 years. One case was reported at birth. There are no familial tendencies and no etiologic clues. X-ray has little therapeutic effect. Cut surfaces of these lesions are an homogeneous grey-white. About 30 or 40 per cent contain some cartilage and various mucinous material. Recurrences can appear as long as 10 years later. In one case in the present series (Case 4) the growth was detected when the patient was 14 years of age. At the time of last report, six years after resection, there was no recurrence.

Malignant Mixed Tumors

In the case of malignant mixed tumors of the parotid area (which are uncommon in children) there is usually a history of a mass that has remained static or indolent for a long time, then has grown rapidly. These lesions are usually larger than benign tumors in the same area and they are usually fixed either to the deeper structures or to the skin. They may be partially encapsulated. Sectioned surfaces appear mushy and friable rather than tough and resilient. The malignant change can be carcinomatous or sarcomatous. Seventh nerve involvement is not common but does occur. Pain is a frequent symptom. The recurrence rate after excision is about 50 per cent. Metastasis to lungs, bones, abdominal viscera and brain has been noted.

For removal, an incision giving adequate exposure is necessary in order that the tumor may be excised with good margins and without spilling the contents. Salivary fistulas occur infrequently and are usually temporary. There was one malignant mixed tumor in our series, in a six-year-old boy (Case 1).

As far as carcinomas in general are concerned, the most common in children, as in adults, is the muco-epidermoid carcinoma. In about one-third of the patients, the tumors persist or recur. Undifferentiated carcinoma is the second most frequent variety in children and it is the most malignant of the juvenile carcinomas in the parotid area.

Although sarcomas are rare, there were two cases in the present series, one case of malignant parotid mesenchymal tumor and one of parotid plexiform neurofibroma with sarcomatous change (Cases 2 and 3).

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